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Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action dated March 17, 2005 (hereinafter, "Office Action").

Claims 14, 15, 20, 31-39, 41-43 and 50-56 are pending in the present application, and these claims currently stand rejected. Applicant respectfully submits that the pending claims are patentable for at least the reasons discussed below.

I. **Claims 14, 15, 20, 31-39, 41-43 and 50-56 Are Patentable in View of Scheele, Cropp and Glass**

Claims 14, 15, 20, 31-39, 41-43 and 50-56¹ stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,863,563 to Scheele (hereinafter, "Scheele") in view of Cropp, Effectiveness of bronchodilators in Cystic Fibrosis, *Am J of Med.* 100(suppl 1A):1A-19S (hereinafter, "Cropp") and U.S. Patent No. 5,162,348 to Glass (hereinafter, "Glass"). More specifically, the Office Action asserts that "it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to employ more than one of the known salts disclosed by Scheele in the therapeutical composition, or treating the patient with a well-known bronchodilator before administering the instant composition." Office Action, page 3. Applicant respectfully disagrees.

A. Scheele is Mischaracterized

Applicant respectfully submits that the Office Action has misconstrued the teachings and relevance of Scheele. The Office Action acknowledges that Scheele does not teach expressly the employment of a combination of salts or the further employment of a bronchodilator in the composition. *See* Office Action, page 2. The Office Action asserts, however, that Scheele "teaches a method for treating symptoms of a patient who has pulmonary conditions, including cystic fibrosis, the method comprising causing the patient to inhale a composition comprising alkali metal salts, such as potassium salt or sodium salts. Various anions may be employed, including bicarbonate." Office Action, page 2, citations omitted.

Scheele discusses a method of treatment that involves "causing a patient to inhale an amount of a pH-raising buffer effective to raise the pH of the aqueous fluid in the microenvironment of the type II alveolar cell luminal surface, thereby inducing an increase in

¹ Claims 1-13, 16-19, 21-30, 40 and 44-49 have previously been canceled without prejudice.

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the rate of surfactant secretion by type II alveolar cells." Scheele, Abstract. Accordingly, Scheele does not teach or suggest at least the highlighted recitations of Claims 14, 51 or 37 presented below.

14. (Previously Presented) A method for treating chronic obstructive pulmonary disease in a subject in need of such treatment, comprising:
administering at least one osmotically active compound to an airway surface of the subject in an amount effective to increase the volume of liquid on the airway surface, wherein the at least one osmotically active compound comprises at least one salt; and
administering a bronchodilator to said subject prior to or concurrently with said osmotically active compound in an amount sufficient to inhibit bronchoconstriction.

51. (Previously Presented) A method for treating cystic fibrosis in a subject in need of such treatment, comprising administering at least one osmotically active compound to an airway surface of the subject in an amount effective to increase the volume of liquid on the airway surface;
wherein the at least one osmotically active compound comprises at least one salt; and
administering a bronchodilator to said subject prior to or concurrently with said osmotically active compound in an amount sufficient to inhibit bronchoconstriction.

37. (Currently Amended) A method for treating chronic obstructive pulmonary disease in a subject in need of such treatment, comprising
administering at least one salt to an airway surface of the subject in an amount effective to increase the volume of liquid on the airway surface;
wherein said at least one salt comprises a combination of different salts; and
wherein said combination of different salts have either (i) a same anion or (ii) a same cation wherein at least one of said anion and said cation are non-absorbable in relation to said airway surface.

Scheele further recites that the exemplary pH-raising buffers include alkali metal salts of common biological buffers. *See* Scheele, Col. 6, lines 1-13. However, the mere listing of common biological buffers does not teach or suggest either an osmotically active compound comprising at least one salt or at least one salt that comprises a combination of different salts. Applicant respectfully submits that Scheele must be considered for its teachings in its totality. The test of obviousness is what the combined teachings of the references would have suggested to those of ordinary skill in the art. *See In re Keller*, 208 U.S.P.Q. 871 (C.C.P.A. 1981) (emphasis added). Moreover, the law requires considering the "whole" of the cited references. *In re Keller* at 881.

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One of ordinary skill in the art would consider Scheele as being directed to a method employing administration of a pH-raising buffer. Accordingly, one of ordinary skill in the art would envision compounds that increase pH and not *per se* osmotically active compound comprising at least one salt or even a combination of different salts. Applicant notes that a pH-raising buffer and an osmotically active compound can represent mutually exclusive compounds.

A pH-raising buffer acts to lower the $[H^+]$. As understood by one of ordinary skill in the art, salts vary in the manner in which they affect pH. For example, a salt comprising an anion of a strong acid and a cation of a weak base may lower the pH of a solution. Thus, osmotically active compounds and combination salt compositions disclosed in the present invention can undermine the goal of raising the pH in an environment presented in Scheele. Further, the pH-raising buffers presented in Scheele may not function in a manner similar to the compounds disclosed in the present application.

Accordingly, Scheele merely describes a method that relates to a patient inhaling an amount of a pH-raising buffer effective to raise the pH of the aqueous fluid in the microenvironment of the type II alveolar cell luminal surface. Scheele fails to teach or suggest a method comprising, among other things, (a) administering at least one osmotically active compound to an airway surface of the subject in an amount effective to increase the volume of liquid on the airway surface wherein the at least one osmotically active compound comprises at least one salt, or (b) administering at least one salt comprising a combination of different salts wherein the combination of different salts have either (i) a same anion or (ii) a same cation wherein at least one of said anion and said cation are non-absorbable in relation to said airway surface. Thus, Scheele points one of ordinary skill in the art in a different direction than the present inventor proceeded.

B. The Combination of Scheele, Cropp and Glass Does Not Teach or Suggest the Present Invention

The Office Action asserts that Cropp and Glass teach that bronchodilators are well known to be useful for treating cystic fibrosis. *See* Office Action, page 3. Cropp and Glass do not, however, cure the deficiency of Scheele in terms of disclosing a method comprising, among other things, administering an osmotically active compound comprising at least one salt as recited in Claims 14 and 51. Cropp and Glass also fail to teach or suggest administering at least one salt comprising a combination of different salts wherein the

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combination of different salts have either (i) a same anion or (ii) a same cation wherein at least one of said anion and said cation are non-absorbable in relation to said airway surface as recited in Claim 37. Accordingly, the combination of Scheele, Cropp and Glass do not lead one of ordinary skill in the art to the present invention as recited in Claims 14 and 51, or Claim 37.

Yet the Office Action further states that "[t]he combining treatment with bronchodilator is also obvious since bronchodilators are known to be useful for treating cystic fibrosis. The optimization of a result effective parameter, e.g., the method of administering two agents, is considered within the skill of the artisan. See In re Boesch and Slaney (CCPA) 205 USPQ 215." Office Action, page 3. Applicant respectfully submits that the cited case law does not support the obviousness rejection of Claims 14, 15, 20, 31-39, 41-43 and 50-56 in view of Scheele, Cropp and Glass.

More specifically, *In re Boesch and Slaney* concerned the obviousness rejection of the ranges of constituents of Appellants' claimed alloys in view of alloys disclosed in the prior art. *In re Boesch and Slaney* at 218. In this instance, the osmotically active compounds comprising at least one salt is not taught or suggested by Scheele, Cropp and/or Glass. Accordingly, methods directed to administering at least one osmotically active compound to an airway surface of the subject wherein the at least one osmotically active compound comprises at least one salt; and administering a bronchodilator as recited in Claims 14 and 51 are not matters of optimizing a result effective parameter. Instead, the recited methods present novel, nonobvious approaches to treating chronic obstructive pulmonary disease (Claim 14) and cystic fibrosis (Claim 51).

Accordingly, Applicant respectfully submits that Claims 14, 15, 20, 31-39, 41-43 and 50-56 are not obvious under 35 U.S.C. § 103(a) in view of Scheele in further view of Cropp and Glass, and respectfully requests that this rejection be withdrawn.

II. **Claims 14, 15, 20, 31-39, 41-43 and 50-56 Are Patentable in View of Scheele, Cropp, Glass and Robinson et al.**

The Office Action alleges that Claims 14, 15, 20, 31-39, 41-43 and 50-56 are obvious in view of Scheele, Cropp and Glass for reasons previously discussed, and Robinson et al., *Effect of Hypertonic Saline, Amiloride, and Cough on Mucociliary Clearance in Patients*

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With Cystic Fibrosis, American Journal of Respiratory and Critical Care Medicine, Vol. 153, 1996, pp. 1503-1509 (hereinafter, "Robinson et al.") provide further motivation to combine the cited references. In particular, the Office Action states that Robinson et al. teaches that "[o]ne of ordinary skill in the art, would have been further motivated to combine a hypertonic solution, such as those disclosed by Scheele with a bronchodilator for treatment of cystic fibrosis patients because of the benefit suggested by Robinson et al." See Office Action, page 4. Applicants respectfully disagree.

In contrast to the assertion of the Office Action, Scheele does not disclose hypertonic solutions. Instead, as noted previously, Scheele describes pH-raising buffers. As understood by one of ordinary skill in the art, a hypertonic solution is one that is characterized as having a high concentration of solute relative to another solution. Examples of hypertonic solutions include, but are not limited to, specific saline solutions, amino acid solutions and dextrose solutions. Thus, "hypertonic solutions" and "pH-raising buffers" are not synonymous or interchangeable terms. Moreover, these terms are not synonymous or interchangeable with the terms "osmotically active agent" or "salt" as recited in the claims of the present application.

In sum, Applicant respectfully submits that a general mention of concomitant usage of therapies with similar indications fails to provide an enabling disclosure to motivate one of ordinary skill in the art to arrive at the osmotically active compounds comprising at least one salt or use of a specific combination of salts as recited in the claims of the present application.

Applicant reiterates that the test of obviousness is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*. In view of the teachings of Scheele directed to the use of pH-raising buffers for performing a specific function in the lumen of type II alveolar cells in comparison to osmotically active compounds and/or salts employed for a distinct physiological purpose, the combination of Scheele, Cropp, Glass and/or Robinson et al. would not have suggested to one of ordinary skill in the art a method for treating chronic obstructive pulmonary disease and/or cystic fibrosis in a subject in need of such treatment as recited in the claims of the present application.

Accordingly, Applicant respectfully submits that Claims 14, 15, 20, 31-44, 50-56 are not obvious under 35 U.S.C. § 103(a) in view of Scheele in further view of the cited references, and respectfully requests that this rejection be withdrawn.

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Conclusion

In view of the foregoing remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,



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Date of Signature: June 11, 2005